

## RESPONSE

Claims 25 to 27 are under examination. Reconsideration is requested.

The Examiner objected to the specification because it did not contain a reference to the priority application. The specification has been amended to insert the required information about the priority application.

### Rejection under 35 U.S.C.112, 1<sup>st</sup> paragraph

Claims 25-27 remain rejected under 35 U.S.C. 112, first paragraph as containing subject matter that was not described in the specification in such a way as to enable a skilled person in art to make and use the invention. The examiner maintains his previous view that the disclosure of the present specification is insufficient to support the scope of the claims since physiological technique is unpredictable. Applicants respectfully traverse the rejections for the following reasons.

A. As Applicants previously stated, the term “stage” has a plain meaning in English language as defined as “a period or step in a progress, activity or development; esp: one of distinguishable periods of growth and development of a plant or animal” (Merriam Webster’s Collegiate Dictionary, tenth edition, Springfield Mass., 1993). The term, therefore, is not limited to the embryonic state but can be applied to any distinguishable stage of embryonic, juvenile or adult stage as is well understood by any person skilled in the art.

In this regard, the examiner states that “the specification fails to teach any stage of organ formation except for embryonic condition of *xenopus*.” The term “stage”, however, is well understood by any person skilled in the art.

The examiner also states that “--- fails to practice any organ culture other than a *xenopus* embryo”, however, it would be impossible, as a matter of fact, to practice for all the animal species. If this is the case, whether it is disclosed to all the species or not should be determined based on the technical background at the time when the application was filed. In this regard, Professor Makoto Asashima who is a person skilled in the art as

well as the present inventor declared in the Declaration that “the principal of basic differentiation such as development, cell differentiation, organ differentiation, and so on, is common to many vertebrates, and same is true of different species.” This comment is technically evidenced. In contrast, the examiner only states that the specification fails to disclose species other than *xenopus* and does not recognize that organ culture other than a *xenopus* embryo cannot be brought into practice. Applicants respectfully submit that it is not appropriate to require this level of experimentation from applicants at the time of filing.

B. The examiner refers to the latest version of Merriam Webster’s Collegiate Dictionary and states that “the terms blastula and blastocyst represent a correspondent stage of the non-mammalian and mammalian embryonic development, and the two are structurally different.” As stated in the section A above, however, the present invention encompasses organs other than *xenopus* embryo so that Applicants respectfully submit that the examiner is missing the point.

C. As mentioned earlier, Professor Makoto Asashima of Tokyo University who is the inventor of the present invention and is an authority in the field of developmental biology declares in the Declaration that “a proficient person in the art can readily (without undue experiments) determine which genomic DNA can be used as a stage marker by an usual protocol such as a differential display method when targeting a particular organ of a particular vertebrate. A researcher of the field will never imagine that the invention as filed cannot be practiced unless a broad range of experiments have been completed for all of amphibians, birds, bony fish, elephant fish Chondrichthyes, mammals, reptiles, and so on”. A person skilled in the art is able to determine a genomic DNA to be used as a stage marker without undue experiment once the vertebrate as a target of the study and its organ is specified, and to culture the organ induced from the ectoderm region excised from blastula of the animal up to the same developmental stage as that of an organ recipient vertebrate, and to transplant to *in vivo* of an animal of the same species by an usual protocol. Conversely, the examiner only argues that the specification contains no

disclosure other than for *xenopus* and he does not argue that stage-specific genomic DNA markers other than for *xenopus* cannot be determined. The examiner's requirement that all the stage-specific genomic DNA markers for additional vertebrates should be determined before filing the application is excessive.

The examiner also states that "the statement is insufficient to maintain to any stage of the life span, neonatal, juvenile and adult, which could mean years of maintaining in a proper culture environment where an matured organ is induced from the ectoderm region of an embryo, such long term organ culture has not been realized even for organs obtained from a fully developed donor". However, as was stated previously that "Applicants respectfully submit that the fact that reports of organogenesis may be scarce in vertebrates other than amphibians is not relevant to the patentability of the present invention. The present methods are new, and the fact that previously described methods may have been more, or less, successful, should not reflect either favorably or unfavorably on the presently claimed method. Applicants have described specific examples of methods that should be successful in mammals as well as in the lower vertebrates, such as *xenopus*. The examiner has presented no convincing reason to doubt applicants' assertions in this regard", the present invention is characterized in that it is a method to carry out transplantation at the corresponded developmental stages, and thus Applicants submit that the examiner is missing the point of Applicants' position.

D. To the above-mentioned statement of Applicants that "The examiner has presented no convincing reason to doubt applicants' assertions in this regard", the examiner states that "the specification only teaches a method of induction and culture of *xenopus* embryo which is no more than a single species among species of the broad genus. A disclosure for a single species does not generally provide a proper base to support generic claims in an application which targets a technical invention the result of which is unpredictable", and cites number of judgments in this regard. Applicants respectfully submit that many US patents have been granted that are contrary to this view of the examiner. Given this fact, the examination practice of the USPTO does not appear to be as determinate as the examiner states.

In view of the above, it is believed the application is in condition for allowance, and Notice to that effect is respectfully requested. If any minor issues remain in the application that might be resolved by a telephone discussion, the Examiner is invited to telephone the undersigned.

Please charge any additional fee deemed due to Deposit Account No. 22-0261 and advise us accordingly.

Respectfully submitted,

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